UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

Jesse McDowell, Plaintiff, v. Eli Lilly and Company, Defendant.	:	13 Civ. 03786 (RWS, GWG) ECF CASE

DEFENDANT'S MEMORANDUM IN SUPPORT OF MOTION FOR SUMMARY JUDGMENT

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INTRODUCTION

An inherent risk of antidepressant treatment is the possibility of adverse symptoms upon cessation of treatment, especially when treatment ends abruptly. This risk is well understood in the medical community and reflected not only in all antidepressant labeling but also in the relevant practice guidelines published by the psychiatric medical community.

Notwithstanding his healthcare practitioner's familiarity with this risk, Plaintiff Jesse McDowell alleges that Eli Lilly and Company ("Lilly") did not adequately warn of the risk of symptoms upon discontinuing Cymbalta, a prescription medicine approved by the FDA to treat major depressive disorder. From the moment FDA first approved Cymbalta in 2004, however, the FDA-approved label for the medicine has included a detailed, three-paragraph warning on risk of discontinuation symptoms. This warning explicitly identifies the same symptoms Mr. McDowell claims he experienced when he completed his Cymbalta treatment — dizziness, headache, fatigue, paresthesia (electric shock sensations), insomnia, and suicidal thoughts. The warning further advises that these symptoms presented at "a significantly higher rate" than placebo patients in the Cymbalta clinical trial experience and provides direction to prescribing medical professionals about safe discontinuation of the medicine.

Despite this longstanding, detailed guidance, Mr. McDowell contends that Cymbalta's warning was inadequate. He further claims that, had the Cymbalta discontinuation warnings been stronger, his original prescriber, Nurse Practitioner Joan Caruana, would not have prescribed Cymbalta for him. The undisputed factual record confirms that all of Mr. McDowell's claims fail, and summary judgment is appropriate on two independent grounds.

First, as this Court has held, "a drug manufacturer will not be liable if there is evidence showing that the warning specifically warned of the side effects which occurred." *Alston v. Caraco Pharmaceutical, Inc.*, 670 F. Supp. 2d 279, 286 (S.D.N.Y. 2009) (Sweet, J.).

The Cymbalta warning on potential discontinuation symptoms provides detailed information on the risks of taking Cymbalta, including the specific potential symptoms possible from terminating Cymbalta treatment — including the very symptoms that Mr. McDowell has alleged. The warning also provides guidance on the safe discontinuation of the medicine.

Second, Mr. McDowell cannot prove a causal link between any alleged deficiency in the Cymbalta discontinuation warning and his claimed injuries. *See Alston*, 670 F. Supp. 2d at 285. Under New York law, Ms. Caruana's testimony that she independently understood the risk of antidepressant discontinuation severs any causal link between Lilly's warning and Mr. McDowell's injury. Ms. Caruana is an experienced mental health practitioner closely familiar with the discontinuation profile of antidepressants, including Cymbalta. Her independent knowledge is "an intervening event relieving the manufacturer of any liability to a patient under the failure to warn theory." *Banker v. Hoehn*, 718 N.Y.S.2d 438, 440-41 (N.Y. App. Div. 2000). Importantly, another federal court has granted summary judgment in a matter involving virtually identical claims where the prescriber similarly testified that he independently appreciated the risk of Cymbalta discontinuation symptoms. *Carnes v. Eli Lilly & Co.*, No. 13-591, 2013 WL 6622915, at *7 (D.S.C. Dec. 16, 2013).

Separately, Ms. Caruana testified that a different discontinuation warning would not have changed her decision to prescribe Cymbalta to Mr. McDowell, a patient with a decade-long history of major depression resistant to the panoply of antidepressant therapies he had tried. The record confirms that Ms. Caruana's decision to prescribe Cymbalta to Mr. McDowell was guided by her extensive clinical experience, not the Cymbalta discontinuation warning. Because "a more stringent warning would have had no practical effect on the [prescriber's] action[]," *Alston*, 670 F. Supp. 2d at 285, Mr. McDowell's claims fail.

FACTUAL BACKGROUND

Mr. McDowell began using Cymbalta at the age of 26 against a complex background of challenging family circumstances, prolonged substance abuse, and longstanding depression that proved resistant to a wide range of medications over the previous eight years.

Raised in Chattanooga, Tennessee, Mr. McDowell confronted significant family issues. His mother used marijuana daily for much of his childhood, his father was an alcoholic who "went to jail a number of times," and his stepfather was physically abusive. (*See* Deposition of Jesse McDowell ("McDowell Dep.") 85:9-16, 20:12-25, 129:14-130:4, attached as Ex. 1 to Declaration of Brett Reynolds ("Reynolds Decl.").)

Mr. McDowell began using marijuana at the age of 11. (McDowell Dep. 83:7-18.) (*See* November 5, 2008 Letter from Josh Torgovnick to Joan Caruana ("Torgovnick Letter"), Reynolds Decl. Ex. 3 at McDowell-Lilly-Caruana,J.-000005.) He began abusing other drugs at the age of 14, eventually using heroin, cocaine, ecstasy, methamphetamines, mushrooms, LSD, prescription painkillers, Ritalin, and Xanax. (*Id.*; *see also* McDowell Dep. at 98:25-99:5, 99:24-100:7.) "If it could be snorted, he did [it]." (Torgovnick Letter.) After years of drug use, Mr. McDowell was concerned enough about his history that, in 2008, he consulted with a neurologist to determine whether his drug use had "injured his brain." (*Id.*) This pattern of substance abuse was mirrored in Mr. McDowell's use of alcohol, which he consumed as "medication" — "a way to not feel, not [to] have emotions." (McDowell Dep. at 81:3-10.)

At approximately the age of 18, Mr. McDowell began treatment for depression. (*Id.* 106:21-107:3.) The depression caused a "lack of motivation or desire to really do anything," (*Id.* 107:21-25) as well as insomnia, a condition that had plagued him "since childhood." *Id.* at 109:6-8; Brooklyn Center for Psychotherapy Records at McDowell-Lilly-BCP-000066, attached as Ex. 8 to Reynolds Decl.) At times, his depressive episodes would leave him feeling "down"

for a month or two at a time. (McDowell Dep. at 108:17-109:5.) Mr. McDowell also experienced migraines, a condition he shared with his parents and sister. (Torgovnick Letter.)

These symptoms persisted when Mr. McDowell moved in 2007 to New York City, where he maintained only sporadic employment as a waiter and was unable to successfully launch a business selling tea. Mr. McDowell "ma[de] just enough to cover [his] bills," paying his landlord and roommate only "whatever [he] could afford," and struggled to make friends. (McDowell Dep. at 31:25-32:5; 49:14-22; 50:5-11; 52:4-6; 52:4-13; 57:18-21.) Mr. McDowell's inability to gain ground professionally contributed to his depressed mood, causing him to experience fear and anxiety over the failure of his business and concern that he could not be happy until he was financially successful. (*See* Brooklyn Center for Psychotherapy Records at McDowell-Lilly-BCP-000092, 94, 104, 106, 123; attached as Ex. 8 to Reynolds Decl.)

By September 2008, when Jesse McDowell first saw Nurse Practitioner Joan Caruana, he had a lengthy, unsuccessful history of trying to manage his depression with prescription antidepressants. (*See* Caruana Medical Records at McDowell-Lilly-Caruana, J.-000004, attached as Ex. 3 to Reynolds Decl.) He had taken Remeron at age 18, Zoloft from ages 18 to 21, Lexapro from ages 22 to 24, a combination of Lexapro and Wellbutrin at age 24, Wellbutrin alone from age 25 to 26, and a combination of Prozac and Wellbutrin starting at age 26, earlier in 2008. (*Id.*) None of those medications brought Mr. McDowell's depression under control. (McDowell Dep. at 140:15-18.) And in his own handwritten description of his history provided to Ms. Caruana, Mr. McDowell reported experiencing problematic side effects from all of these medications. (Reynolds Decl. Ex. 3 at McDowell-Lilly-Caruana, J.-000004.) On Remeron, he slept for 14 hours a day and felt like a "zombie;" on Zoloft he had "no energy and little sleep," with a "very monotone state" with "no emotion;" on Lexapro, he was "overly

emotional" and tired; adding Wellbutrin to Lexapro made him feel "over-medicated" with poor sleep; Wellbutrin alone left him still feeling "down;" a combination of Effexor and Wellbutrin caused "many side effects," especially a "tight feeling" in his head; finally, on Prozac and Wellbutrin, he experienced feelings of paranoia and sleeplessness. (*Id.*; *see also* McDowell Dep. 131-139.)

After consulting with Mr. McDowell about his condition and history, Ms. Caruana decided to add Cymbalta to his therapeutic regimen. (Deposition of Joan Caruana ("Caruana Dep.") at 18:10-24, attached as Ex. 2 to Reynolds Decl.) She chose Cymbalta due to Mr. McDowell's "relative lack of success with some of the other medicines." (Caruana Dep. at 31:8-12.) Ms. Caruana directed him to discontinue Prozac, and to take 20-30 milligrams of Cymbalta along with Wellbutrin as well as Klonopin as needed for panic attacks. (Caruana Dep. at 21:2-16.) On November 3 of that year, she increased Mr. McDowell's dose of Cymbalta to 60 milligrams. (*Id.* at 23:13-14) Throughout November and December, Ms. Caruana and Mr. McDowell continued to "tinker" with his medications, adjusting his prescriptions for Seroquel, Wellbutrin, and Zyprexa to help his insomnia, grogginess, and depression. (*Id.* at 24:23-27:07.) By March 2009, Ms. Caruana discontinued Zyprexa to alleviate Mr. McDowell's acne. (*Id.* at 28:03-11.) On April 8, 2009, Mr. McDowell's last visit with Ms. Caruana, she increased his dosage of Cymbalta to 90 milligrams. (*Id.* at 28:14-29:05.) Mr. McDowell continued to fill his Cymbalta prescriptions, written by other healthcare providers, until 2012. (*See* Thriftway Pharmacy Records at 2-8, attached as Ex. 6 to Reynolds Decl.)

In the fall of 2008, the full prescribing information for Cymbalta (the "package insert" or the "label") included an explicit warning on discontinuation symptoms:

> 5 WARNINGS AND PRECAUTIONS
>
> . . . .

> 5.6 Discontinuation of Treatment with Cymbalta
>
> Discontinuation symptoms have been systematically evaluated in patients taking duloxetine. Following abrupt or tapered discontinuation in placebo-controlled clinical trials, the following symptoms occurred at a rate greater than or equal to 1% and at a significantly higher rate in duloxetine-treated patients compared to those discontinuing from placebo: dizziness, nausea, headache, fatigue, paresthesia, vomiting, irritability, nightmares, insomnia, diarrhea, anxiety, hyperhidrosis and vertigo.
>
> During marketing of other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. Although these events are generally self-limiting, some have been reported to be severe.
>
> Patients should be monitored for these symptoms when discontinuing treatment with Cymbalta. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate *[see Dosage and Administration (2.4)]*.

(Cymbalta Physician Packet Insert (June 2008), Caruana Dep. Ex. 2, attached as Ex. 4 to Reynolds Decl.)

The package insert also contained a warning in the "Highlights" section on the first page, cautioning that discontinuation of Cymbalta "[m]ay result in symptoms, including dizziness, nausea, headache, fatigue, paresthesia, vomiting, irritability, nightmares, insomnia, diarrhea, anxiety, hyperhidrosis, and vertigo." (*Id.*) Separately, the label warned of the risk of suicidal thoughts, including upon discontinuation:

> All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior,

> especially during the initial few months of a course of drug therapy, *or at times of dose changes, either increases of decreases*.

(*Id.* at Section 5.1) (emphasis added).

After years as a nurse practitioner treating patients with mood disorders, Ms. Caruana independently understood the potential risk of discontinuation symptoms described in the Cymbalta label. (Caruana Dep. at 38:19-23.) Indeed, she was familiar with the widely-held clinical understanding that "[d]iscontinuation symptoms are common following antidepressant treatment." (David G. Perahia et al., *Symptoms following abrupt discontinuation of duloxetine treatment in patients with major depressive disorder*, 89 J. of Affective Disorders 207 (2005), attached as Ex. 5 to Reynolds Decl. (hereinafter "2005 JAD Article"); *see also* Caruana Dep. at 33:23-25 ("There are symptoms that are going to occur if you . . . discontinue [an antidepressant] abruptly.").) Ms. Caruana testified that, in her experience, "most patients" who abruptly stop taking antidepressants like Cymbalta suffer discontinuation symptoms. (Caruana Dep. at 33:12-14; *see also id.* at 41:14-15 ("I would say at least half [experience symptoms].").)

In March 2012, Mr. McDowell told his then-psychiatrist, Dr. Jacob Messing, that he wanted to try to manage his depression without medicine. (McDowell Dep. at 156:19-22.) Consistent with a widespread appreciation of the risks associated with stopping antidepressants, Dr. Messing advised Mr. McDowell to taper off of Cymbalta over a seven-month period. (Compl. ¶ 32; *see also* McDowell Dep. at 156:2-18.) Not only is such guidance consistent with Cymbalta's label and those of other antidepressants, but it is spelled out expressly in the psychiatric community's applicable practice guidelines. (*See* Reynolds Decl. Ex. 4 at Section 5.6; *id.* Ex. 9 at 20 (American Psychiatric Association Practice Guideline for the Treatment of Patients With Major Depressive Disorder) ("When pharmacotherapy is being discontinued, it is best to taper the medication over the course of at least several weeks. To minimize the

likelihood of discontinuation symptoms, patients should be advised not to stop medications abruptly . . . .").)

Mr. McDowell alleges that he experienced a constellation of symptoms following his discontinuation, including "extreme brain zaps," "frequent suicidal thoughts," "bouts of insomnia," "debilitating headaches," and "a constant state of dizziness." (*See* Plaintiff's Answers and Objections to Defendant's First Set of Interrogatories, Reynolds Decl. Ex. 7 at 6.) Mr. McDowell never sought treatment for any of these symptoms, nor could he recall that he had ever mentioned them to any physician. (McDowell Dep. 166:18-20.) Mr. McDowell testified that the "brain zaps" had ended by the spring of 2013, that the dizziness subsided within four months of discontinuing Cymbalta, and that his headaches stopped within a week of discontinuing Cymbalta. (McDowell Dep. at 170:22-171:17.) He no longer suffers any of the discontinuation symptoms that he has alleged. (*Id.* at 178:7-10.)

ARGUMENT

Summary judgment is appropriate where "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a) (2010). To defeat a summary judgment motion, "[t]he nonmoving party must come forward with specific facts showing that there is a *genuine issue* for trial." *Higazy v. Templeton,* 505 F.3d 161, 169 (2d Cir. 2007) (quoting *Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 586-87 (1986).) "Conclusory allegations, conjecture, and speculation . . . are insufficient to create a genuine issue of fact." *Kerzer v. Kingly Mfg.*, 156 F.3d 396, 400 (2d Cir. 1998). Rather, to survive summary judgment, the party opposing the motion must prove there is sufficient evidence to support a jury verdict in its favor. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 249 (1986). Summary judgment is appropriate where "the record taken as a whole could not lead a rational trier of fact to find for the non-moving party." *Matsushita*, 475 U.S. at 587.

I. The Cymbalta Discontinuation Warning Is Adequate As a Matter of Law.

Under New York law, a manufacturer's duty to warn of the risks of a prescription medicine runs to the prescribing medical professional, not an individual patient. *See Martin v. Hacker*, 628 N.E.2d 1308, 1311 (N.Y. 1993) ("Warnings for prescription drugs are intended for the physician . . . . [T]he manufacturer's duty to caution against a drug's side effects is fulfilled by giving adequate warning through the prescribing physician, not directly to the patient."). Having discharged this duty, the manufacturer may not be held liable for product liability claims stemming from the patient's use of the drug. Because Lilly provided an adequate warning regarding the potential risks of Cymbalta discontinuation, summary judgment is warranted.

A. Lilly's Duty to Warn Runs to Prescribing Medical Professionals.

Under well-established New York law, Lilly has a duty to warn prescribing medical professionals of "potential dangers in its prescription drugs that it knew, or, in the exercise of reasonable care, should have known to exist." *Martin*, 628 N.E.2d at 1311. This duty applies to failure to warn claims based both in strict liability and negligence. *See Mulhall v. Hannafin*, 841 N.Y.S.2d 282, 285 (N.Y. App. Div. 2007). Under this "informed intermediary" doctrine, "the manufacturer's duty to caution against a drug's side effects is fulfilled by giving adequate warning through the prescribing physician, *not* directly to the patient." *Martin*, 628 N.E.2d at 1311 (emphasis added); *see also Spensieri v. Lasky*, 723 N.E.2d 544, 549 (N.Y. 1999). The prescriber, "whose duty it is to balance the risks against the benefits of various drugs and treatments and to prescribe them and supervise their effects," is thus the "informed intermediary" between the manufacturer and the individual patient. *Martin*, 628 N.E.2d at 1311; *see also Wolfgruber v. Upjohn Co.*, 423 N.Y.S.2d 95, 96 (N.Y. App. Div. 1979) *aff'd*, 52 N.Y.2d 768 (N.Y. 1980); *Ames v. Apothecon, Inc.,* 431 F. Supp. 2d 566, 573 (D. Md. 2006) (physicians "are presumed to have considerable medical training as well as the ability to access the medical

literature if they require additional information"). The adequacy of the warning provided to a prescriber may be determined as a matter of law. *See, e.g.*, *Martin v. Hacker*, 628 N.E.2d 1308, 1312 (N.Y. 1993).

B. The Cymbalta Label Expressly Warned of Discontinuation Symptoms.

Since Cymbalta's initial 2004 approval for the treatment of major depressive disorder, the FDA-approved label for the medicine has included an explicit, three-paragraph warning on the risk of symptoms upon discontinuation of Cymbalta therapy. That warning has included a clear statement about the occurrence of discontinuation symptoms in the Cymbalta clinical trial experience, including the important fact that the rate was significantly higher in Cymbalta patients than patients on placebo; a recitation of the specific symptoms possible upon Cymbalta discontinuation (including the precise symptoms alleged by Mr. McDowell); and guidance on the appropriate protocol for safe discontinuation of the medicine. This comprehensive warning is legally adequate as a matter of New York law.

"It has long been the law in New York that prescription medicine warnings are adequate when, as here, information regarding 'the precise malady incurred' was communicated in the prescribing information." *Alston*, 670 F. Supp. 2d at 284 (quoting *Wolfgruber*, 423 N.Y.S.2d at 96-97). A warning is adequate as a matter of law "if it provides specific detailed information on the risks of the drug." *Martin*, 628 N.E.2d at 1312. In making this determination, the Court should consider factors including "whether the warning is accurate, clear, consistent on its face, and whether it portrays with sufficient intensity the risk involved in taking the drug." *Id.* A warning is clear if it is "direct, unequivocal and sufficiently forceful to convey the risk." *Id.* at 1313. The warning should also be evaluated as a whole and not through the nitpicking prism of an interested legal advocate after the fact:

> While a meticulous examination and parsing of individual sentences in the insert may arguably reveal differing nuances in meaning or variations in emphasis as to the seriousness of a side effect, any resulting vagueness may be overcome if, when read as a whole, the warning conveys a meaning as to the consequences that is unmistakable.

Id.

Federal courts applying New York law routinely apply this standard. *See, e.g.*, *Yates v. Ortho-McNeil-Janssen Pharm., Inc.*, No. 3:09-oe-40023, 2014 WL 1369466, at *5 (N.D. Ohio Apr. 7, 2014) (Katz, J.) (applying New York law) ("Because the document explicitly warned that the product could cause strokes, the Court finds that the warning is sufficient to meet the Defendants' duty to provide adequate warnings to treating physicians regarding a possible risk of the product."); *In Re Accutane Prods. Liab.*, MDL No. 1626, 2012 WL 3194954, at *1, **4-5 (M.D. Fla. July 24, 2012) (Moody, J.) (applying New York law) ("The Physician Package Insert plainly and prominently identified inflammatory bowel disease by name as a *possible consequence of taking Accutane*. This risk information appeared in the 'WARNINGS' and 'ADVERSE REACTIONS' sections of the insert. It also identified the common symptoms of IBD and instructed what should be done if those symptoms appeared.") (emphasis in the original). This standard is reflected in the law of virtually every state, and Courts routinely dispose of such cases at the dispositive motion stage.[1] In sum, "[w]here the warning given to the

[1] *See, e.g., Meridia Prods. Liab. Litig.*, 447 F.3d 861, 867 (6th Cir. 2006) (concluding that Meridia's blood pressure warning was adequate because it was "accurate, clear, and unambiguous"); *Ziliak v. AstraZeneca LP*, 324 F.3d 518, 521 (7th Cir. 2003) (concluding that Pulmicort's warning about glaucoma and cataracts was adequate under Indiana law); *Ehlis v. Shire Richwood, Inc.*, 367 F.3d 1013, 1018 (8th Cir. 2004) (applying North Dakota law) (holding warning that Adderall may exacerbate "behavior disturbance and thought disorder" and warning of "psychotic episodes" adequate to warn of Adderall-induced homicidal/suicidal psychosis); *Dash v. Roche Labs.*, No. 94-55814, 1996 U.S. App. LEXIS 983, at *7 (9th Cir. Jan. 11, 1996) (applying California law and holding Accutane warning of persistent dry eye adequate and stating that "[a] written warning is adequate if it directly warns in plain and explicit terms of the (continued…)

prescribing physician by the manufacturer through the Physician's Desk Reference (PDR), package inserts and other literature gives specific detailed information on the risks of the drug, the manufacturer has been held absolved from liability as a matter of law." *Wolfgruber*, 423 N.Y.S. 2d at 97.

As set forth below, the elements of the Cymbalta discontinuation warning "portray[] with sufficient intensity the risk involved in taking the drug," 628 N.E.2d at 1312.

Highlights of Prescribing Information.

The Highlights of Prescribing Information section of the Cymbalta label in effect at the time of Mr. McDowell's initial prescription warns that discontinuation "[m]ay result in symptoms, including dizziness, nausea, headache, fatigue, paresthesia, vomiting, irritability, nightmares, insomnia, diarrhea, anxiety, hyperhidrosis, and vertigo." (*See* Reynolds Decl. Ex. 4 at 1.)

Dosage and Administration.

The Dosage and Administration section of the Cymbalta label explicitly warns that "[s]ymptoms associated with discontinuation of Cymbalta and other SSRIs and SNRIs have been reported. A gradual reduction in the dose rather than abrupt cessation is recommended

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specific risk that has caused injury to plaintiff."); *In re Chantix (Varenicline) Prods. Liab. Litig.*, 881 F. Supp. 2d at 1340-43 (concluding that Chantix's warning about neuropsychiatric injuries was adequate as a matter of law); *Reece v. Astrazeneca Pharms., LP*, 500 F. Supp. 2d 736, 748-51 (S.D. Ohio 2007) (concluding that Crestor's warning about rhabdomyolysis was adequate under Ohio law); *Ames v. Apothecon, Inc.,* 431 F. Supp. 2d 566, 569, 573 (D. Md. 2006) (applying Maryland law) (concluding that warning in "Adverse Reactions" section that "[t]he following adverse reactions have been reported as associated with the use of penicillin ... toxic epidermal necrolysis" was adequate); *Brumley v. Pfizer, Inc.*, 149 F. Supp. 2d 305, 312 (S.D. Tex. 2001) (concluding that Viagra's warning regarding the risks of the drug for patients with heart disease was adequate under Texas law); *Gurski v. Wyeth-Ayerst Div. of Am. Home Prods. Corp.*, 986 F. Supp. 654, 654-55 (D. Mass. 1997) (concluding that Triphasil 21's warnings about liver tumors were adequate under Massachusetts law).

whenever possible" and directs prescribers to the more detailed warning provided in the label's Warnings and Precautions section. (*See* Reynolds Decl. Ex. 4 at 4.)

Warnings and Precautions.

The Warnings and Precautions section of the Cymbalta label additionally provides thorough and complete detail of the risks of discontinuation symptoms.

Clear statement of risk. The Cymbalta label plainly sets out the risk of symptoms arising from "abrupt or tapered discontinuation" and warns that, in placebo-controlled clinical trials, discontinuation symptoms occurred "at a significantly higher rate in duloxetine-treated patients compared to those discontinuing from placebo." (Reynolds Decl. Ex. 4 at 8.) *See Gurski v. Wyeth-Ayerst Div. of Amer. Home Prods. Corp.*, 986 F. Supp. 654, 654 (D. Mass. 1997) (granting summary judgment where warning "cautioned the plaintiff specifically regarding the probability, nature, and gravity of the precise condition that she sufficiently suffered").

Detailed identification of possible symptoms. The Cymbalta label includes a detailed catalog of symptoms possible upon discontinuation. Indeed, the very symptoms Mr. McDowell alleges that he experienced after stopping his Cymbalta treatment are identified in the discontinuation warning. *See Alston*, 670 F. Supp. 2d at 284 ("[P]rescription medicine warnings are adequate when, as here, information regarding 'the precise malady incurred' was communicated in the prescribing information.") (quoting *Wolfgruber*, 423 N.Y.S.2d at 96-97).

During the period relevant here, the label included approximately a dozen symptoms occurring "at a rate greater than or equal to 1%" in placebo-controlled clinical trials for Cymbalta: "dizziness, nausea, headache, fatigue, paresthesia, vomiting, irritability, nightmares, insomnia, diarrhea, anxiety, hyperhidrosis and vertigo." (Reynolds Decl. Ex. 4 at 8.) This method of communicating information on individual symptoms appearing in clinical trials

is consistent with the accepted practice of identifying such individual adverse events observed at or above a specified threshold and in accord with FDA regulations and guidance directing that the label "list the adverse reactions identified in clinical trials that occurred at or above a specified rate appropriate to the safety database." 21 C.F.R. § 201.57(c)(7); *see also* FDA, *Guidance for Industry: Adverse Reactions Section of Labeling for Human Prescription Drug and Biological Products–Content and Format* (Jan. 2006). In addition, the label has consistently included an additional subset of potential symptoms reported upon discontinuation of products within the SNRI class to which Cymbalta belongs and warns that "patients should be monitored" for all of the symptoms identified in the warning. (Reynolds Decl. Ex. 4 at 8.)

Section 5.1 of the Warnings and Precautions in the Cymbalta label additionally provides a thorough and complete account of the clinical worsening and suicide risks attendant to taking antidepressants, including in the case of downward adjustments in the dosage of an antidepressant. (*Id.* at 5-6.) The label warns:

> All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, *or at times of dose changes, either increases or decreases*.

(*Id.* at 6 (emphasis added).) These suicidality warnings are shared by all antidepressants and are well-known in the medical community. (*See* FDA, Public Health Advisory: Suicidality in Adults Being Treated With Antidepressant Medications (June 30, 2005).[2])

Potential severity. The discontinuation warning explicitly speaks to the "severity" and "duration" of potential discontinuation symptoms within the SNRI class: "Although these

[2] *Available at* http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/PublicHealthAdvisories/ucm053169.htm.

events are generally self-limiting, some have been reported to be severe." (*Id.*) More fundamentally, the label specifically identifies symptoms that, by their nature, have the capacity to be severe and that are not, by definition, self-limiting. This clear statement of risk appears in the label's WARNINGS and PRECAUTIONS section, which, by law, must include all "clinically significant adverse reactions (including any that are potentially fatal, are serious even if infrequent)." 21 C.F.R. § 201.57(c)(6); *see also Ames*, 431 F. Supp. 2d at 569 n.9 (recounting opinion of plaintiffs' expert that "most 'serious' adverse reactions are listed in the Warnings section"); *Martin*, 628 N.E.2d at 1312 (noting that Warnings section "deals with side effects of graver consequences than the Adverse Reactions section").

Protocol for safe discontinuation. The Cymbalta discontinuation warning devotes a paragraph to advising prescribers of the appropriate means of taking a patient off the medicine. Section 5.1 of Warnings and Precautions advises in connection with the suicidality warning, "If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that discontinuation can be associated with certain symptoms." (Reynolds Decl. Ex. 4 at 6.) Section 5.6 states: "Patients should be monitored for these symptoms when discontinuing treatment with Cymbalta. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered." (Reynolds Decl. Ex. 4 at 8.)

Taken together, this comprehensive warning is adequate as a matter of law because it is "accurate, clear, consistent on its face" and "portrays with sufficient intensity the risk involved in taking the drug." *See Martin*, 628 N.E.2d at 1312.

II. Mr. McDowell Cannot Establish Proximate Cause.

Even if Mr. McDowell were able to overcome this threshold bar to his claims, summary judgment would nevertheless be appropriate because he cannot establish that any alleged inadequacy in the Cymbalta discontinuation warning was the proximate cause of his injuries. Two distinct grounds support this conclusion. *First*, Mr. McDowell's initial Cymbalta prescriber, Ms. Caruana, had independent knowledge of the risks of discontinuation symptoms based upon her training and experience with depression patients. *Second*, the summary judgment record establishes that had Cymbalta's labeling been different, Ms. Caruana would not have changed her decision to prescribe the medicine to Mr. McDowell. Either of these grounds is independently sufficient under New York law to break the chain of proximate causation.

A. Ms. Caruana Independently Understood Cymbalta's Discontinuation Risks.

Under New York law, "where the treating physician is independently aware" of potential adverse events, that knowledge is "an intervening event relieving the manufacturer of any liability to a patient under the failure to warn theory." *Banker v. Hoehn*, 718 N.Y.S.2d 438, 440-41 (N.Y. App. Div. 2000); *see also Alston*, 670 F. Supp. 2d at 286 (S.D.N.Y. 2009) ("The Plaintiff has not shown that a failure to warn . . . was the proximate cause of his injuries, as his physicians were aware of the risks . . ."); *Figueroa v. Boston Scientific Corp.*, 254 F. Supp. 2d 361, 370 (S.D.N.Y. 2003). A physician's existing awareness of a potential risk or side effect thus "sever[s] the causal [chain]" between an allegedly inadequate warning and a plaintiff's injury. *Glucksman v. Halsey Drug Co.*, 553 N.Y.S.2d 724, 726 (N.Y. App. Div. 1990).

Here, it is beyond dispute that Ms. Caruana had independent knowledge of (1) the risk of antidepressant discontinuation symptoms, including with Cymbalta; (2) the specific symptoms possible upon abrupt discontinuation; and (3) the potential frequency of events.

Knowledge of Risk of Discontinuation Symptoms. Ms. Caruana testified that, based on her clinical experience and training, she was aware of the risk of discontinuation symptoms with abrupt cessation of Cymbalta treatment:

> Q. [I]s it fair to say that based on your over 20 years working . . . as a nurse practitioner . . . in the psychiatric area, that you have an understanding of the risks that can occur when a person stops taking an anti-depressant like Cymbalta?
>
> . . . .
>
> A. I know that most patients who stop abruptly . . . are going to get symptoms of stopping abruptly.
>
> Q. And . . . how do you know that?
>
> A. Because patients report it to me.
>
> Q. Is it fair to say that there's an understanding in the psychiatric community that there are risks associated with discontinuing an antidepressant?
>
> . . . .
>
> A. There are symptoms that are going to occur . . . if you discontinue abruptly.
>
> Q. [You'd] want to wean or taper someone off a medicine to minimize the chance of those symptoms?
>
> A. Right.

(Caruana Dep. at 33:04-34:08.)

> Q. Let me ask you to look under "[d]osage and administration [on the Cymbalta label]," which is on the left-hand column. … There[] looks like four bullet points [and a] chart. … The final bullet point says "[d]iscontinuing Cymbalta[,] [a] gradual dose reduction is recommended." … [Y]ou see that?
>
> A. Yes.
>
> Q. Is that what you were talking about earlier?
>
> A. Yes.

. . . .

Q. That's something you knew about in your general practice[ ] as opposed to, you know, what was written here?

A. Yes.

(Caruana Dep. at 38:02-23 .)

Awareness of Specific Discontinuation Symptoms. Upon reviewing the discontinuation symptoms listed on Cymbalta's label during her deposition, Ms. Caruana testified that she was independently aware of the specific symptoms described in the label:

Q. [L]ooks like the sixth bullet in that section under "[w]arnings and precautions," it says as follows: "Discontinuation may result in symptoms including dizziness, nausea, headache, fatigue, paresthesia, vomiting, irritability, nightmares, insomnia, diarrhea, anxiety, hyperhidrosis, and vertigo[.]" … [D]o you see that?

A. Yes.

Q. [I]s that information that you were generally aware of as it related to Cymbalta?

A. Yes.

. . . .

Q. There's a word there called "paresthesia"[?]

A. Yes.

Q. Tell the jury what paresthesia is.

A. Paresthesia is strange feelings or -- it can be tingling, it can be numbness in the hands or feet or elsewhere[] in the arms or legs.

Q. Can it sometimes . . . be described in lay terms as an electric shock sensation?

A. [Y]es.

Q. And that's something that…

A. [That's something that] occurs very frequently with abrupt [cessation] of any of the SSRIs.

(Caruana Dep. at 39:13-40:24.)

Frequency of Discontinuation Symptoms. In describing her clinical experience with SSRIs and SNRIs, Ms. Caruana testified that "at least half" of her patients experience some discontinuation symptom upon an abrupt cessation of treatment. (Caruana Dep. at 41:05-19.) With respect to paresthesia, the "electric shock" sensation, Ms. Caruana testified that they occur "very frequently" upon discontinuation. (Caruana Dep. at 40:22-24.) When confronted with the specific data on discontinuation symptoms reflected in the 2005 JAD Article on the rate of patients with discontinuation symptoms upon abrupt discontinuation in the reported studies — 44.3% on Cymbalta and 22.9% on placebo — Ms. Caruana volunteered that she had "seen that . . . many people have those problems." (Caruana Dep. at 58:10-11.)

This acknowledgment is critical here. Mr. McDowell's central claim in this lawsuit is that Lilly misled medical professionals about the rate of discontinuation symptoms by listing the events seen in the clinical trials "at a rate greater than or equal to 1%," consistent with the Federal Regulations. *See* 21 C.F.R. § 201.57(c)(7)(ii)(A). To be clear, Lilly submits that this theory is legally deficient to establish liability and that there is nothing improper about failing to list specific rates for individual discontinuation adverse reactions. Indeed, no other antidepressant provides such detailed information in its labeling.[3] But more fundamentally, Plaintiffs' gimmick theory has no applicability here because Ms. Caruana expressly testified that she was not misled in the way Plaintiffs suggest:

> Q. . . . Does that mean to you that there's only a 1 percent chance of any of this thing — any of these things happening?
>
> A. No.

[3] *See* Reynolds Decl. ¶ 11.

(Caruana Dep. at 47:14-18.)

New York law holds that a prescriber's independent knowledge of the risks of a drug or medical device breaks the chain of proximate causation. In *Ohuche v. Merck & Co.,* 903 F. Supp. 2d 143 (S.D.N.Y. 2012), for example, the physician who had prescribed the plaintiff a vaccine for shingles "testified at deposition that she was aware of the adverse reactions associated with ZOSTAVAX." *Id.* at 151. The manufacturer's alleged failure to adequately disclose the risks of the drug, therefore, was not the proximate cause of the plaintiff's injuries. *Id.* at 151-52. Similarly, in *Banker v. Hoehn*, "there [was] no question" that the treating physician "was fully cognizant of the potential of hypertrophic scarring" from the use of an argon laser to treat a facial birthmark. 718 N.Y.S.2d at 441. That knowledge was an "intervening event" in the causal chain which "reliev[ed] the manufacturer of any liability to a patient under the failure to warn theory." *Id.* at 440-41. *See also Figueroa*, 254 F. Supp. 2d at 370 (holding that no proximate causation existed where "a treating physician is well aware of the risks of a medical device, independent of any warning by the manufacturer"); *Glucksman*, 553 N.Y.S.2d at 726-27 (holding that plaintiff could not show proximate cause where treating physician had independent knowledge of the risks posed by treatment, because "physician's decision not to inform the plaintiff of the risk . . . was an intervening cause.").

Another federal court has recently held that a prescribing physician's independent knowledge of potential Cymbalta discontinuation symptoms made it impossible for the plaintiffs to establish proximate cause. *See Carnes*, 2013 WL 6622915, at *7. There, the plaintiffs, represented by the same lawyers as in this case, made allegations virtually identical to those raised in this suit, including the claim that the "1%" figure in the Cymbalta label was misleading. Because the prescribing doctor in *Carnes* had "independent knowledge of the risk of withdrawal

symptoms through his training and experience" and independent of the Cymbalta label, the court ruled that plaintiffs could not prove proximate cause. *Id.* at *5-6.

So too here. Ms. Caruana testified unequivocally that that she had knowledge of the risks of abrupt discontinuation independent of the information provided by Lilly and and that she was not misled in the manner on which Plaintiff hinges his claim. Thus, Lilly did not proximately cause Mr. McDowell's injuries and is "reliev[ed] . . . of any liability" under Mr. McDowell's theory. *Banker*, 718 N.Y.S.2d at 441. *See also Porterfield v. Ethicon, Inc.*, 183 F.3d 464, 468 (5th Cir. 1999) (no proximate cause where physician was independently aware of possible risks of using medical device through experience and review of literature); *Odom v. G.D. Searle & Co.*, 979 F.2d 1001, 1003 (4th Cir. 1992) ("[T]he manufacturer cannot be said to have caused the injury if the doctor already knew of the medical risk."); *Kirsch v. Picker, Int'l, Inc.*, 753 F.2d 670, 671 (8th Cir. 1985) ("Picker's failure to warn Dr. Murphy could not have been the proximate cause of Kirsch's injury if Murphy was already aware of the cancer risks associated with radiation therapy."); *Ames v. Apothecon, Inc.*, 431 F. Supp. 2d 566, 573 (D. Md. 2006) ("[T]he warnings are intended to be read by learned intermediaries who are presumed to have considerable medical training as well as the ability to access the medical literature if they require additional information.").

B. A Different Discontinuation Warning Would Not Have Changed Ms. Caruana's Prescribing Decision.

There is a separate, independent factual basis for concluding that proximate cause cannot be established: Ms. Caruana's testimony that a different discontinuation warning in the Cymbalta label would not have changed her prescribing decision. Under New York's proximate cause standard, "a plaintiff must demonstrate that had a different, more accurate warning[] been given, his physician would not have prescribed the drug in the same manner." *Alston*, 670 F.

Supp. 2d at 285. *See also Mulhall v. Hannafin*, 841 N.Y.S. 2d 282, 45 A.D.3d 55, 60-61 (N.Y. App. Div. 2007) ("[P]laintiffs had to show that had the warning been different, Dr. Hannafin would have departed from her normal practice and used another device."). Courts across the country have applied the same standard.[4] Summary judgment is appropriate where a plaintiff fails to present evidence that a prescribing physician's decision to prescribe a particular medication would have changed had a different warning been given. *Mulhall*, 45 A.D.3d at 61. *See also Erony v. Alza Corp.*, 913 F. Supp. 195, 200 (S.D.N.Y. 1995) ("An act cannot be the 'substantial cause' if the injury would have occurred regardless of the content of defendant's warning.").

In her deposition, Ms. Caruana testified explicitly that a different warning containing the very information Plaintiffs allege was missing from the Cymbalta labeling would not have changed her decision to prescribe Cymbalta to Mr. McDowell:

> Q. If the physician package insert, the prescribing information[,] had said not that the following symptoms occur[ ]at a rate equal to . . . or greater than . . . one percent, but it said that these events occur in at least one patient in the clinical trials 44.3 percent of the time while they occur in placebo discontinuation 22.9 percent of the time, *would that have [had] any impact on your decision to use Cymbalta*?
>
> A. *No*[.] [B]ecause in actual practice, we're talking about discontinuation and I've seen that many people have those problems.

[4] *See, e.g.*, *Wheat v. Pfizer, Inc.*, 31 F.3d 340, 343 (5th Cir. 1994) ("Plaintiffs must demonstrate that '. . . but for the inadequate warning, the treating physician would not have used or prescribed the product.'"); *Motus v. Pfizer, Inc.*, 196 F. Supp. 2d 984, 997-98 (C.D. Cal. 2001) (granting summary judgment where no evidence that prescribing physician would not have prescribed medicine to plaintiff given a different warning), *aff'd*, 358 F.3d 659 (9th Cir. 2004); *Hoffman-La Roche Inc. v. Mason*, 27 So. 3d 75, 76 (Fla. Dist. Ct. App. 2009) (per curiam) ("Because Appellee presented no evidence from either treating physician that a differently worded warning would have resulted in either physician not prescribing Accutane for his extreme acne, Appellee failed to establish that the allegedly deficient warning was the proximate cause of his injury therefore, we reverse.").

(Caruana Dep. at 57:20-58:11(emphasis added).) Indeed, Ms. Caruana stands by her prescription of Cymbalta to Mr. McDowell, explaining that she currently has 20-25 patients to whom she is prescribing Cymbalta. (Caruana Dep. 22:4-12, 71:8-9.)

Even under examination by Mr. McDowell's attorney, when asked whether information that discontinuation symptoms occurred in "40 to 50 percent" of patients in clinical studies would impact her decision to prescribe Cymbalta, Ms. Caruana testified that "it would affect not the prescribing so much." (Caruana Dep. at 129:02-03.) Ms. Caruana did testify that if the rate were indeed so high (in contrast to her own experience), she might have decided to emphasize to patients the importance of tapering off of Cymbalta (*Id.* at 129:04-12), but she did *not* say that it would have impacted her prescribing decision. Not having received the answer he was hoping for on this front, Mr. McDowell's attorney continued to press the point with Ms. Caruana, who explained that she relies on her clinical experience more than labeling language:

> Q. And that's why I'm asking … if you had been provided this information in 2008, what would that have done in your mind in comparing [the effects of] Cymbalta [to other drugs,] with respect to withdrawals specifically?
>
> . . .
>
> A. I'd still have to go with my experience with patients[,] [s]o that would temper what I'm reading here [about discontinuation risk] . . . [b]ecause my experience with patients doesn't lead me to believe that it is in the same league [as Effexor's high rate of discontinuation symptoms].

(Caruana Dep. at 132:13-25.)[5]

[5] Although Ms. Caruana testified that "if [she] knew that [withdrawal from Cymbalta] could be potentially as severe as the withdrawal from Effexor, [another antidepressant therapy,] then [she] would choose something else," (Caruana Dep. at 138:12-14), there is nothing in the record establishing that Cymbalta's discontinuation profile is comparable to Effexor's. To the contrary, Ms. Caruana distinguished Effexor as "the one drug [she] really dislike[s] because of the discontinuation syndrome that happens almost on a daily basis if you don't take it on time . . . ," (continued…)

Because Mr. McDowell cannot demonstrate that a different warning would have changed Ms. Caruana's prescribing decision, summary judgment is warranted. *Alston*, 670 F. Supp. 2d at 285. *See also Motus v. Pfizer, Inc.*, 358 F.3d 659, 661 (9th Cir. 2004) ("[A] product defect claim based on insufficient warnings cannot survive summary judgment if stronger warnings would not have altered the conduct of the prescribing physician."); *Solomon v. Bristol-Myers Squibb Co.*, 916 F. Supp. 2d 556, 570 (D.N.J. 2013) (granting summary judgment where prescribing physicians "represented that they would [not] have . . . changed their prescription for Plaintiff even understanding the additional risks or questions of efficacy Plaintiff . . . raised"); *Carnes*, 2013 WL 6622915, at *6-*7 (granting summary judgment where prescribing physicians testified that they still would have prescribed Cymbalta had they been presented with a stronger warning); *Hoffman-La Roche Inc. v. Mason*, 27 So. 3d at 77 (Fla. Dist. Ct. App. 2009) (no proximate cause where physician testified that he would still have prescribed the medicine even if he had plaintiff's proposed better warning).

III. Mr. McDowell's Failure-to-Warn Claims Subsume His Remaining Claims.

Mr. McDowell's laundry list of tag-along claims[6] must also fail in the face of Cymbalta's legally adequate warning. *See In Re Accutane*, 2012 WL 3194954 at *6 ("[U]nder New York law, the adequacy of the warnings, as a matter of law, precludes any related claims for negligence, strict liability, breach of warranties, or fraud."). As an initial matter, New York does not recognize a design defect theory of liability for prescription medicines. *See Martin*, 628

(Caruana Dep. at 76:21-24), and testified that in her experience with Cymbalta (which she estimated she has prescribed to over 100 patients), Cymbalta "is [not] in the same league" as Effexor on discontinuation symptoms. (Caruana Dep. at 29:14-17; 132:13-25.)

[6] (*See* Compl. ¶¶ 48-64 (defective design); ¶¶ 41-47 (negligence); ¶¶ 81-91 (breach of implied warranty); ¶¶ 92-103 (negligent misrepresentation); ¶¶ 104-114 (fraud); ¶¶ 115-130 (violation of consumer fraud laws).)

N.E.2d at 1311 ("[A] prescribed drug, accompanied by adequate warnings, is "not defective, nor is it unreasonably dangerous.") (internal quotation marks and citation omitted).

More fundamentally, a plaintiff cannot simply recast his warning theory in terms of "warranty" or "fraud" to avoid the legal implications of an adequate warning. For that reason, courts ruling in pharmaceutical cases routinely dismiss these tag-along claims on the grounds that warnings were adequate. *See, e.g., In re Norplant Contraceptive Prods. Liab. Litig.*, 955 F. Supp. 700, 709 (E.D. Tex. 1997) (granting summary judgment on all claims because "[t]he gravamen of all of Plaintiffs' causes of action . . . is that Wyeth failed to adequately warn of or disclose the severity of Norplant's side effects"), *aff'd* 165 F.3d 374 (5th Cir. 1999); *Ames*, 431 F. Supp. 2d at 567-68 (D. Md. 2006) (granting summary judgment based on proximate cause and stating defective design, marketing defect, breach of implied warranty, and negligence claims can be "reduce[d] down" to failure to warn claims); *Jack v. Glaxo Wellcome Inc.*, 239 F. Supp. 2d 1308, 1320-22 (N.D. Ga. 2002) (holding the learned intermediary doctrine, as adopted by Georgia courts, insulated a defendant from liability for negligence, strict liability, and breach of implied warranty claims).

And finally, all of Plaintiffs' theories of course still require that he show proximate cause, and, as set forth above, he simply cannot do so.

CONCLUSION

For the foregoing reasons, Lilly's motion for summary judgment should be granted, and judgment entered in Lilly's favor as to all of Plaintiff's claims.

Dated: Washington, D.C.
July 7, 2014

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